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REMARKS/ARGUMENTS

Claims 7-11 and 13-16 are pending; Claims 1-6 and 12 are canceled. Claim 16 is withdrawn from consideration. Reconsideration of the rejections is requested.

The presently pending claims have been rejected as anticipated or made obvious by Rodan *et al.*, U.S. Patent no. 5,780,291. Applicants respectfully submit that the cited art fails to teach a method of isolating a biologically active, substantially homogeneous composition of Wnt protein comprising a lipid moiety.

Applicants respectfully submit that the cited art does not teach the presently claimed methods. It is noted that the cited document is silent as to the hydrophobic nature of Wnt proteins, and to the presence of a lipid moiety.

The Examiner has questioned the previously submitted Declaration made by Dr. Willert. Applicants wish to note that there is no reason to doubt the veracity of the statements provided in the 132 Declaration, and respectfully submit that such should be accepted in the absence of evidence to the contrary.

In particular, a question was raised as to the presumed validity of the Rodan *et al.* claims. As Applicants have previously argued, the ability of Rodan *et al.* to isolate a particular protein is not being questioned; it is the biological activity of the isolate that is lacking in the prior art description.

Certainly one cannot assume that a polypeptide must have a biological activity in order to be isolated and claimed in a patent. Indeed, the case law argues that such activity is not a required element. One may look to Appeal No. 2004-2314, Ex Parte Friedberg *et al,* which found that the ability of a peptide to act as an immunogen was sufficient utility for a patent claim. It is therefore improper to assume that the claims of Rodan *et al.* inherently claim a biologically active protein composition.

The difficulty in isolation of Wnt proteins is well-known in the art. For example, one may look to the attached review by Jeffrey Miller (Genome Biology 2001 3(1):reviews3001.1-3001.15), which states at page 2 "very little is known about the structure of Wnt proteins as they are notoriously insoluble". The attached article by Logan and Nusse (Annu. Rev. Cell Dev. Biol. 2004, 20:781-810) further discusses the point, stating at page 783 that "although Wnt proteins are secreted, difficulties in solubilizing active Wnt molecules had hindered attempts to purify the Wnts and precluded a thorough biochemical characterization of this growth factor family. The insoluble nature of Wnts has now been explained by the discovery that these proteins are

palmitoylated and are more hydrophobic that initially predicted from the primary amino acid sequence."

Applicants note the publication by the inventors of the present application in the international peer-reviewed journal, Nature. As stated in the abstract of Willert *et al.* (2003) Nature 423:448-452, "Wnt proteins are potentially important reagents in expanding specific cell types, but in contrast to other developmental signaling molceuls such as hedgehog proteins and the bone morphogenetic proteins, Wnt proteins have never been isolated in an active form. Although Wnt proteins are secreted from cells, secretion is usually inefficient and previous attempts to characterize Wnt proteins have been hampered by their high degree of insolubility."

Applicants respectfully submit that one of skill in the art is aware of these publications in well-respected journals, and would be aware that Wnt proteins are insoluble when dialyzed into PBS, and therefore the teachings of Rodan *et al.* would not lead to a composition of isolated and biologically active Wnt.

With respect to the specific Wnt protein described by Rodan *et al*, Applicants have attempted to search the scientific literature for evidence of this protein and its possible biological activity. However, a search of Pubmed and of human genome sequences has failed to yield any indication of a "wnt-x" gene; nor has Rodan *et al.* published any articles relating to wnt proteins. A BLAST sequence comparison of the protein claimed in US 5,780,291, performed against all known sequences in Genbank reveals a single match in the patents database, corresponding to the '291 patent sequence listing, however no perfect match was found in any other sequence, *e.g.* in the human genome sequence, or in the genecard database, which provides information for known human genetic loci. It seems that the Wnt-x protein may be related to Wnt-2b, with which it has 96% sequence identity.

On the basis of such a high degree of sequence similarity, Applicants submit that one of skill in the art would believe that the proposed "wnt-x" protein would share the properties of the known protein, Wnt2b, and as such would be insoluble when dialyzed against PBS in the absence of detergent. It is respectfully submitted that the cited art does not teach the isolation of biologically active Wnt protein, and does not anticipate or make obvious the claims of the present application.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

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The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STAN-299.

Respectfully submitted,
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